ATTACHMENT A
Remarks

Claims 3 and 4 are pending in the present application. By this Amendment, Applicants have canceled claims 1 and 2 and amended claim 3. Applicants respectfully submit that the present application is in condition for allowance based on the discussion with follows.

In the Office Action, there was an initial comment regarding the priority claim of the present application, but this comment reflects that the Examiner is not aware of the applicable rules concerning National Stage applications and the priority therefrom. In particular, the passage cited by the Examiner, 37 CFR 1.78(a)(2), only requires that the application be amended to claim reference to co-pending US non-provisional applications or International application designating the US if such applications are claimed for priority. Contrary to the Examiner's statements, the present application IS an International application designating the US (as the National Stage application is considered the same application, only the National phase of the International application), and is NOT an application claiming benefit from such an application. As such, no such reference in the specification is necessary to properly claim priority, and the priority application for the present case, namely Japanese application 11-95654 filed April 2, 1999, was properly received during the International phase of the present application as reflected in the attached Form PCT/IB/304. If the Examiner has any questions with regard to the validity of the claim of priority in the present case, it is requested that the Examiner contact a Supervisory Examiner before repeating the statement regarding priority which is inapplicable to the present application.

In the Official Action, Claims 1 and 2 were rejected under the judicially created doctrine of obviousness-double patenting in view of claims 1-6 of U.S. Patent No. 6,413,495. Without addressing the merits of this rejection, Applicants have canceled claims 1 and 2 rendering the double patenting rejection now moot.

Claims 3 and 4 were rejected under 35 U.S.C. § 112, second paragraph. With regard to the insufficient antecedent basis rejections of claim 3, Applicants respectfully submit that the amendment to claim 3 obviates the insufficient antecedent basis rejections to claim 3.

With regard to the rejection of claim 3 for reciting "such a supporting force which is generated by said inflated balloon to be exerted on the balloon catheter and on the inner wall of the blood vessel at such angioplasty-treated site", Applicants respectfully submit that claim 3 (currently amended) is fully supported by the specification and the claims. By this Amendment, Applicants have removed the word "such" before the "supporting force". As currently recited, a force generated by the inflated balloon is exerted on the balloon catheter and on an inner wall of a blood vessel. Thus, Applicants respectfully submit that the claimed supporting force is not relative and is fully supported by the specification and claims, including the full recitation of claim 3. Therefore, Applicants respectfully request that the rejection to claims 3 and 4 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claims 1 and 2 were rejected under 35 U.S.C. § 102(b) as being anticipated by Mori et al (hereinafter "Mori") and Aizawa et al (hereinafter "Aizawa"). As noted above in response to the double patenting rejection, by this Amendment, Applicants have

canceled claims 1 and 2, thus rendering the § 102(b) rejection of claims 1 and 2 also now moot.

Claims 3 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Aizawa in view of Narciso Jr. U.S. Patent No. 5,298,018 (hereinafter "Narciso"). The Examiner alleges that Aizawa teaches the use of Npe6 during an intravascular catheterization procedure where the Npe6 is administered locally to an atherosclerotic lesion of interest in the intima of a blood vessel and subsequently, the region is exposed to laser beams to provide therapeutic effects. The Examiner admits that Aizawa fails to specifically describe the method during a percutaneous Transuluminal Coronary Angioplasty procedure (PTCA). However, the Examiner alleges Narciso teaches photodynamic therapy during a PTCA procedure to limit restenosis of a blood vessel intima subject to a smooth muscle cell proliferation.

Contrary to the Examiner's allegation, claims 3 and 4 are not obvious from Aizawa in view of Narciso as the references individually or in combination with one another fail to teach or suggest all claimed elements.

The present invention is directed to a photodynamic therapy method. This method includes in part, intravascular irradiation of light by means of an intravascularly inserted laser-irradiating device of a "balloon catheter". The intravascular irradiation of the light is carried out through an inflated balloon which exerts a force to aid in the positioning of the device and to firmly support the catheter on the inner wall of the vascular vessel at the angioplasty-dilated site of the vascular vessel. Preferably, the conditions are such that the bloodstream cannot flow between the inner wall of the vessel and the ballooned wall of the inflated balloon which results in an efficient and

stable irradiation of light onto the inner wall of the vessel at the angioplasty-dilated site of the vascular vessel.

Referring specifically to claim 3, claim 3 recites in part:

> "allowing a central axis of the laser-irradiating optical fiber present within the central and longitudinal hole of said balloon catheter to be held coincidently with and in the same position as the central axis of the vascular lumen of the blood vessel at the angioplasty-treated site of the blood vessel, with aid of a supporting force which is generated by said inflated balloon and is exerted on the balloon catheter and on the inner wall of the blood vessel at said angioplasty-treated site, with the supporting force maintaining said inflated balloon in tight contact with the inner wall of the blood vessel at the treated site, so as to intercept the bloodstream to be flown between the inflated balloon and the inner wall of the blood vessel at the treated site;
>
> and irradiating the compound of formula (I) having accumulated in the interior of the blood vessel wall positioned at the angioplasty-treated site of the blood vessel, with a laser light of an appropriate wavelength, by transmitting from a laser-generator the laser light via said optical fiber in the balloon catheter, in a manner that the transmitted laser light is emitted outwardly from the laser-emitting part at the front end of said optical fiber and is made to pass through the liquid medium present in the inflated balloon and through the wall material of said inflated balloon of the balloon catheter which is in tight contact with the inner wall of the blood vessel, so that the emitted laser light irradiates the compound of formula (I) present in the blood vessel inner wall, whereby said compound so irradiated is photoactivated and allowed to generate and exert the suppressive effects thereof against the thickening of the vascular intima in the angioplasty-treated site of the blood vessel." (Emphasis added.)

Thus, the central axis of the laser-irradiating optical fiber is held coincidental with and in the same position as the central axis of the vascular lumen of the blood vessel at the angioplasty-treated site of the blood vessel with the aid of a supporting force which is generated by the inflated balloon and exerted it on the balloon catheter and on the inner wall of the blood vessel at the angioplasty-treated site. As a result, the optical fiber will be automatically centered within the blood vessel. Further, the inflated balloon intercepts the bloodstream between the inflated balloon and the inner wall of the blood

vessel. In addition, the laser-light is emitted through the wall material of the inflated balloon of the balloon catheter in order to irradiate the compound of formula I present in the blood vessel at the angioplasty-treated site.

For a more complete discussion of the present invention, reference is made to the specification for exemplary purposes only. The specification notes that the present method is achieved as a result of satisfying the following three criteria: 1) a balloon catheter has a balloon membrane which is made of a laser transmissive material; 2) the central axis of the internal optical fiber for transmission of the irradiating light can be held coincidently with and in the same position as that of the central axis of the vascular lumen by inflating the balloon so that irradiating laser light emitted from the optical fiber is applied evenly to the blood vessel inner wall and 3) the bloodstream flow can be stopped in the blood vessel by the inflated balloon.

Referring to Figure 2 of the present specification, the claimed position of the catheter in the blood vessel can be achieved by using the balloon catheter (1) with a completely inflated balloon (2'), of which the top surface has been brought into a close contact with the inner wall (5') of the blood vessel (5) as a result of being pressed outwardly under the resulting hydraulic pressure of the inflating liquid. The completely inflated balloon (2') exerts a force for supporting the optical fiber (3). Thus, the laser-irradiating device as a whole is allowed to be located firmly in the interior of the blood vessel in such way that the central axis of the optical fiber (3) can be held and maintained coincidently with and in the same position as that of the central axis of the vascular lumen of the blood vessel. (See present specification, page 27, line 24 to page 28, line 15).

Finally, page 40, lines 1-14 which refers to Table 1 (page 39) confirms that the present optical fiber with balloon catheter is capable of suppressing the effects of vascular restenosis at the angioplasty-treated site.

Thus, the present invention provides a method which provides suppressive effects of vascular restenosis at the angioplasty-treated site.

Narciso teaches the administration of a photosensitizer which may be made after an angioplasty procedure in order to prevent the growth factor from stimulating the SMC proliferation that can bring about restenosis.

Narciso fails to teach or suggest using a balloon catheter inflated to exert force on an inner wall of a blood vessel thereby allowing a central axis of a laser-irradiating optic fiber to be held coincidentally with and in the same position as the central axis of the vascular lumen of the blood vessel at a angioplasty-treated site of a blood vessel. Although Narciso teaches three constructions for light delivery depending on the lesion to be treated including a balloon catheter which can be inflated in the area of the lesion, Narciso fails to teach or suggest positioning the laser-irradiating optic fiber along the central axis of the vascular lumen and using the aid of a supporting force from an inflated balloon of a balloon catheter, as claimed. As discussed above, the claimed coincidental position of the optical fiber ensures that the optical device is centered within the blood vessel.

Furthermore, although, arguendo, Narciso may teach, in one form, inflating the balloon catheter to totally occlude blood in order to minimize attenuation of therapeutic light in the blood, see, e.g., Narciso, column 8, lines 58-67, Narciso fails to teach or

suggest using a balloon catheter to properly position a laser irradiating optic fiber as claimed.

Moreover, Narciso fails to teach or suggest emitting laser light through a balloon catheter membrane to irradiate a light-absorbing compound disposed at an angioplasty-treated site. On the contrary, Narciso merely teaches emitting light from the end of its optical fiber, in a direction parallel to the catheter, i.e., in an axial direction, not in a radial direction, as occurs when the laser light is emitted through the balloon catheter of the present method.

In summary, the prior art fails to teach or suggest the novel, technical feature of the present invention which includes an inflated balloon which is inserted in the vascular lumen, and which, during the intravascular irradiation, is kept in a close or tight contact with the inner wall of the blood vessel at the angioplasty-treated site, resulting in the interception of the flow of light-absorbing bloodstream between the inflated balloon outer wall and the inner wall of the blood vessel at the angioplasty-treated site and leading to the intravascular irradiation of the laser light at the blood vessel inner wall in an even, stable manner, thereby obtaining an enhanced therapeutic effects of the photo-activated photosensitizer present for suppressing an inducible restosis of the blood vessel at the treated site.

Based on the foregoing discussion, Applicants respectfully submit that claims 3 and 4 are not obvious in view of the cited art, and that the Examiner's rejection on this basis has been respectfully traversed.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance.

END REMARKS